Attorney Docket No. 41577-323890 (P1362)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: **JANE LOUISE HOLLEY**	)
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U.S. Serial No. **10/559,148**	) Art Unit: **1645**
	)
Filing Date: **August 17, 2006**	) Examiner: **Albert Mark Navarro**
	)
For: **COMPOSITIONS COMPRISING LARGE AND SMALL BINDING FRAGMENTS OF ANTIBODIES AGAINST THE SAME TOXIN**	)

DECLARATION UNDER 37 C.F.R. §1.132 OF JANE LOUISE HOLLEY

I, Jane Louise Holley, do hereby declare:

1. I have a Bsc (Hons) degree in Biochemistry with Toxicology from the University of Surrey in Guildford, United Kingdom and a Ph.D. in Biochemistry from the School of Pharmacy in London, United Kingdom. I worked as a Research Scientist at the School of Pharmacy for several years before joining the Department of Biomedical Sciences at the Dstl facility of the UK Ministry of Defence, where I have worked for the past 15 years. I am now a Principal Scientist at Dstl and have numerous peer reviewed publications in the field of microbiology and biochemistry.

2. I am an inventor of the subject matter claimed in U.S. Patent Application Serial No. 10/559,148 ("the present application"). I am familiar with the Office Actions of record in the present application.

3. I declare that the data, attached as Figure S1 and Figure S2, were collected from experiments conducted by me or under my direction. The attached data were generated using experimental procedures similar to those described in Examples 1 and 2 of the present application (page 9, line 19, to page 11, line 13) except that the antisera were raised against

toxoids of ricin toxin and the test animals were challenged with ricin toxin. The ratio of antitoxins used was 50:50.

4. Figure S1 is a graph of weight loss (as a percentage of animal starting weight) as a function of time after intraperitoneal exposure to 1μg ricin and subsequent treatment with antitoxin compositions at two hours after exposure to ricin. The data in Figure S1 show that throughout the 14 days of the experiment, those animals treated with a composition comprising a large binding fragment and a small binding fragment of anti-ricin antibodies experienced less weight loss than those animals treated with a large binding fragment of anti-ricin antibodies alone.

5. Figure S2 is a graph of mean symptom scores of infected animals (using a slightly different symptom scoring system to that described in Example 1 of the present application to reflect the differences in the toxins' mechanisms of action) as a function of time in days post-intraperitoneal challenge with ricin toxin. The animals were treated with two different pharmaceutical compositions at two hours post-exposure to ricin and monitored for signs of intoxication for 14 days. These data clearly show that, on average, animals treated with a composition comprising a large binding fragment together with a small binding fragment of anti-ricin antibodies were less susceptible to the visible signs of intoxication than those animals treated with large binding fragments alone.

6. These data show that using a composition comprising a large binding fragment of an anti-ricin antibody together with a small binding fragment of an anti-ricin antibody is effective in treating ricin poisoning and is also effective as a therapy that provides improved weight loss and intoxication characteristics.

7. I further declare that botulinum toxin, as described in the present application, is a neurotoxin, derived from the Gram positive bacterium *Clostridium botulinum,* and is known to block neurotransmitter release at peripheral cholinergic nerve terminals. Ricin toxin, on

the other hand, is a potent cytotoxin, derived from the castor oil plant, *Ricinus communis*, which inhibits cellular protein synthesis. This is known to one of skill in the art.

8. As one of ordinary skill in the art, I declare that the data provided herein, together with the examples provided in the present application, show that a composition comprising a large binding fragment of an antibody together with a small binding fragment of an antibody is effective against toxins which have different origins and that have completely different modes of action in the intoxicated subject.

9. I declare further that all statements made herein are of my own knowledge and are true, and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine, or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of any patent issuing on this application.

Signature

DR JANE HOLLEY
Name

26 February 2008
Date

Figure S1:

Post exposure therapies administered to mice, in accordance with Example 1 of the present application, 2 hours after systemic (intraperitoneal) challenge with 1 μg ricin. Body weight loss as a function of time (days).

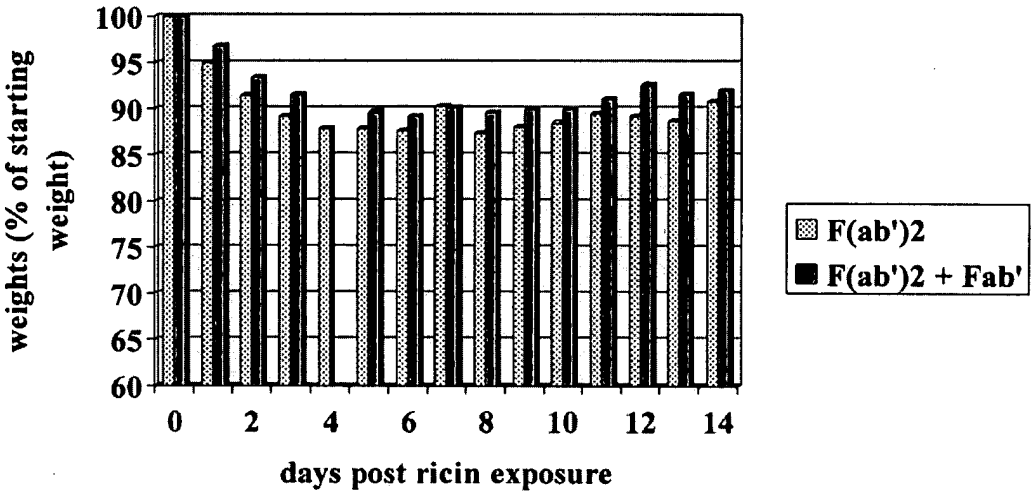

Figure S2:

Post exposure therapies administered to mice, in accordance with Example 1 of the present application, 2 hours after systemic (intraperitoneal) challenge with 1 μg ricin. Mean Symptom Scores.

0 normal
1 mild piloerection
2 medium piloerection
3 severe piloerection